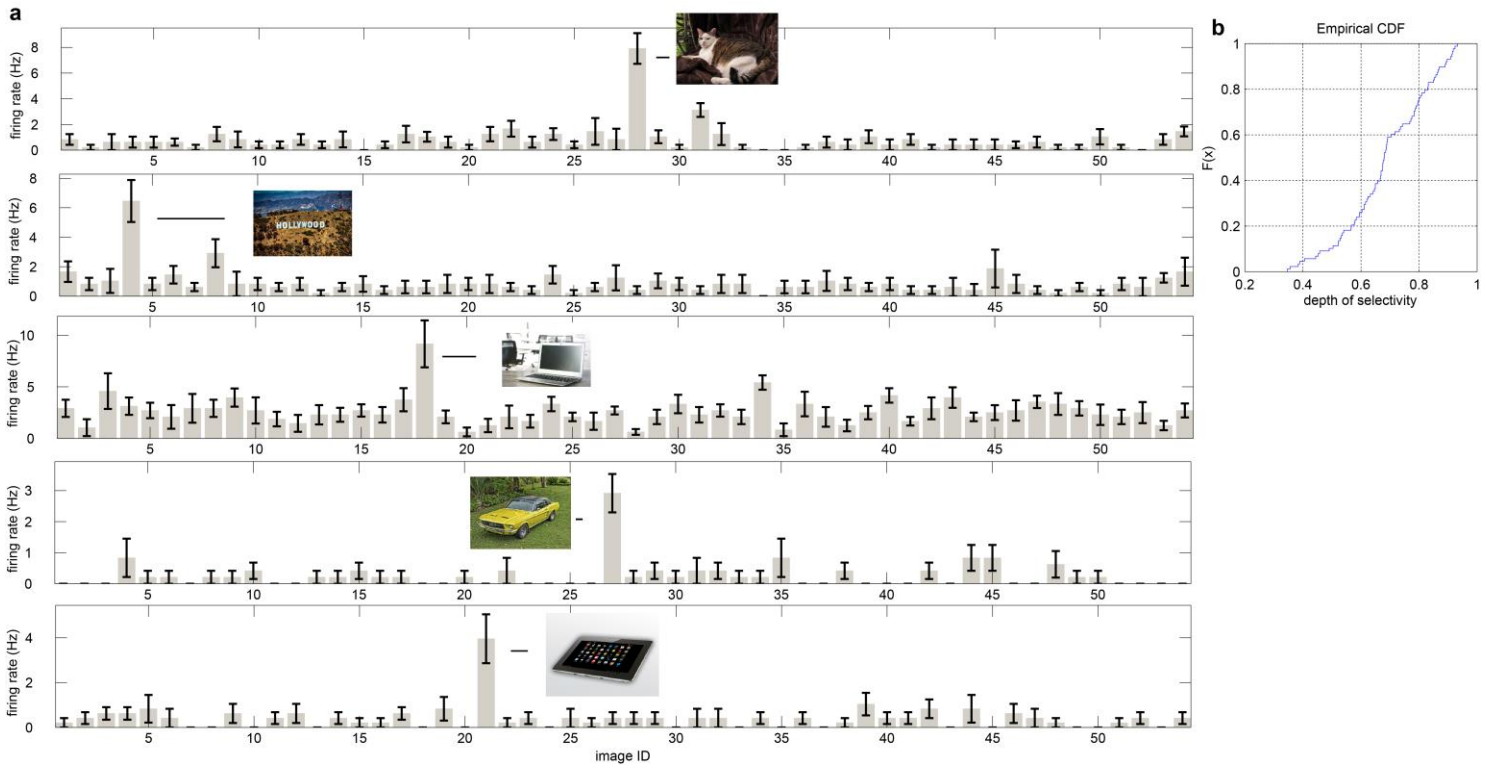
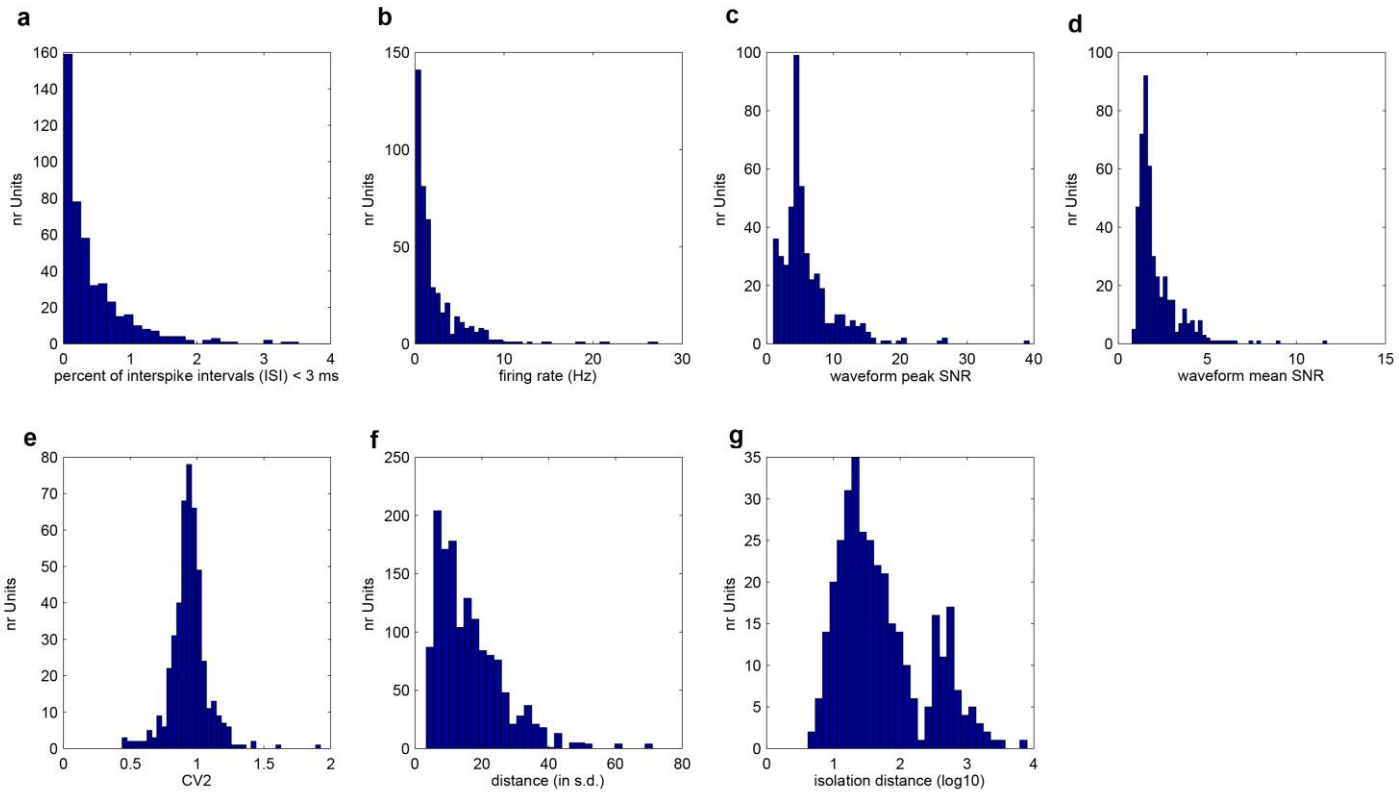


Supplementary Figure 1

Tuning of concept cells in MTL during the screening task.

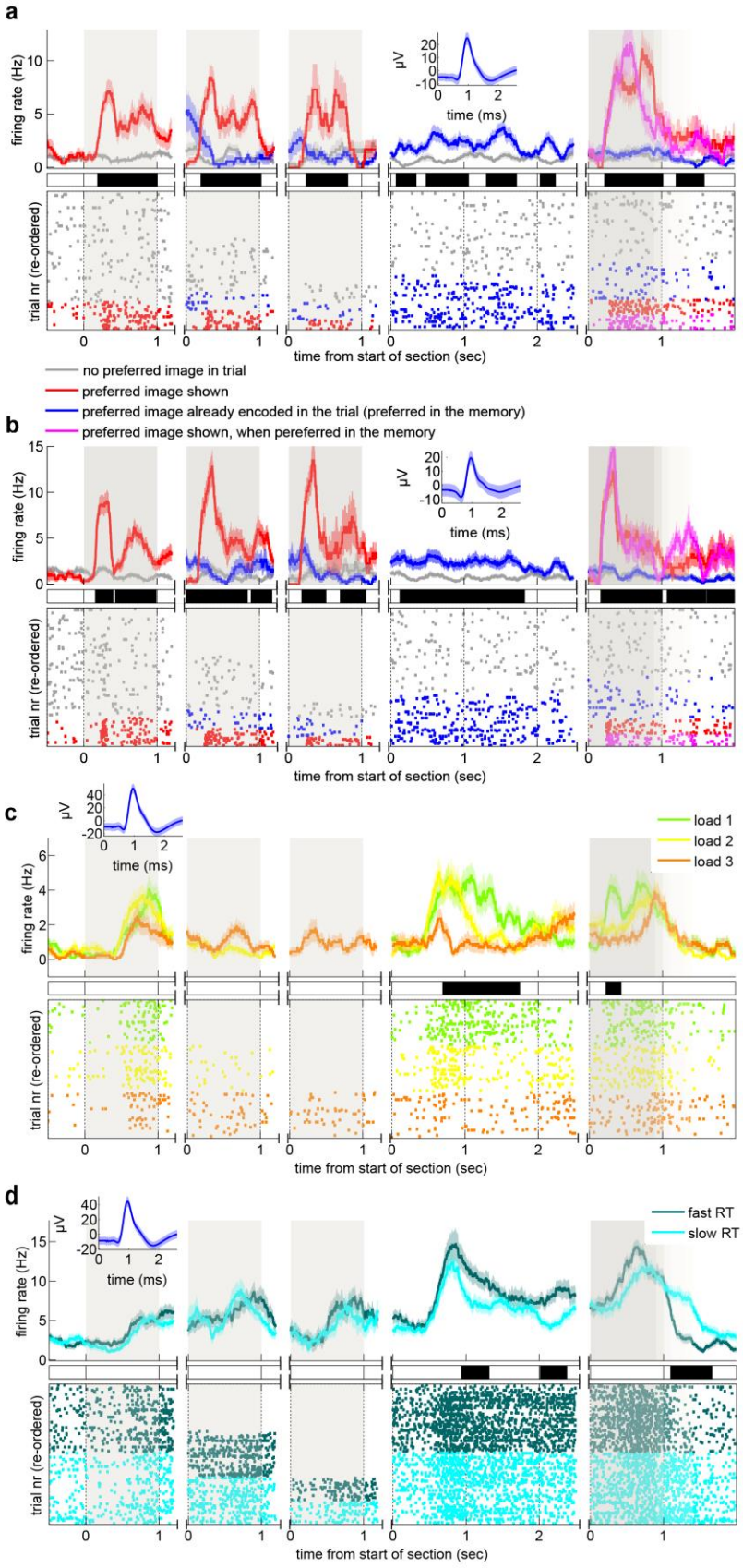
(a) Examples of responses of five neurons classified as concept cells for the 54 tested images. Error bars represent ±s.e. across the 6 presentations of each image. The image shown in each panel represents the picture with the highest response. (b) Cumulative distribution of the depth of selectivity (S) index for all concept cells identified in the screening task (N=88). The average DOS of 0.68 indicates a sparse response. Note that some of the example images shown are different from those shown to patients due to copyright issues.



Supplementary Figure 2

Spike-quality metrics for all identified putative single-cells (clusters).

(a) Histogram of proportion of inter-spike intervals (ISIs) that were shorter than 3ms. The large majority of clusters had less than 0.5% of such short ISIs. (b) Histogram of average firing rate. (c) Histogram of the singal-to-noise ratio (SNR) of the peak of the mean waveform. (d) SNR of the whole waveform of all units. (e) Histogram of coefficient-of- variation (CV2) values for every neuron. (f) Pairwise distance, estimated using the projection test, between clusters where more than one unit was found on one wire. (g) Isolation distance for all units for which this metric was defined (median = 30.9).



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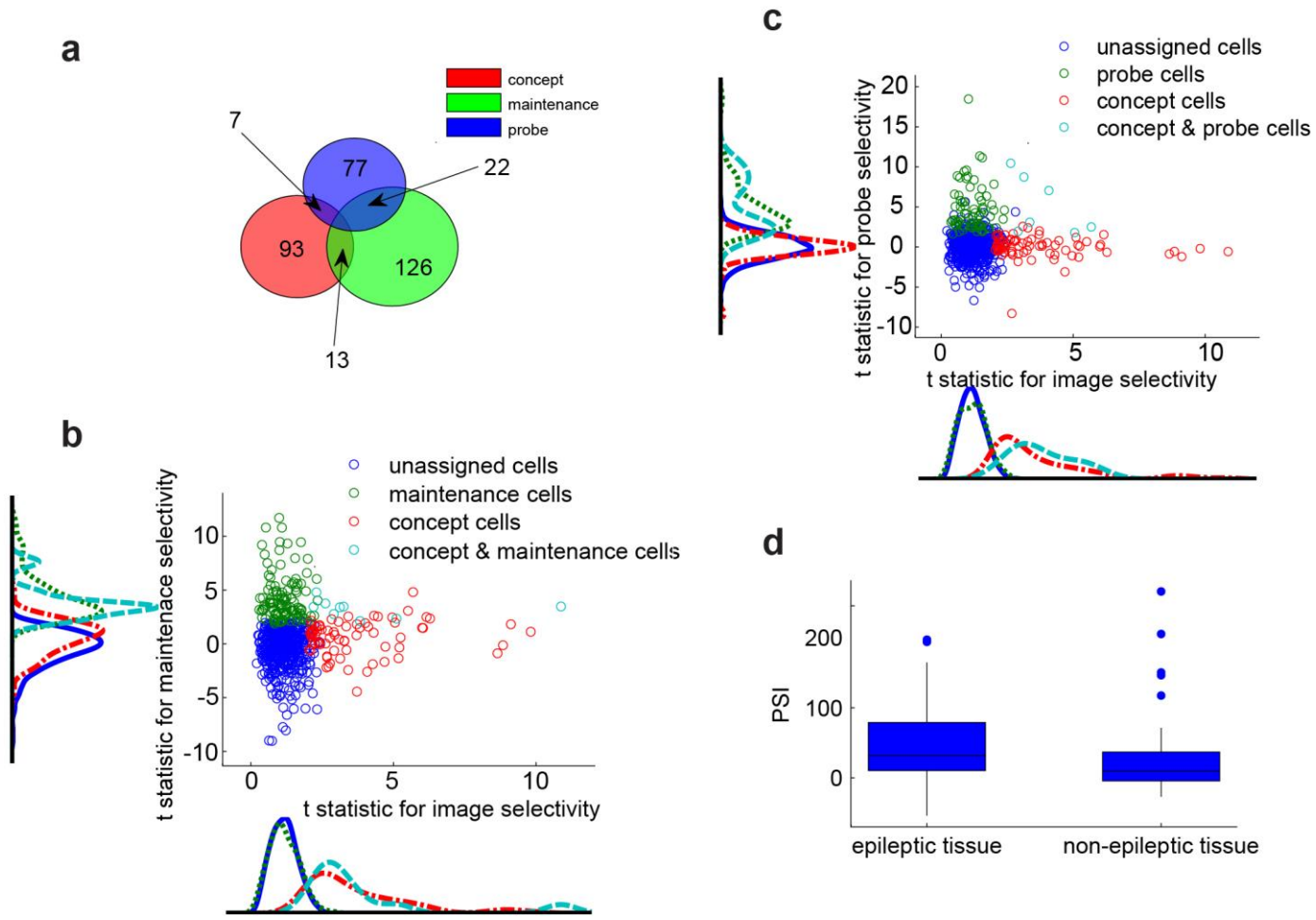
Supplementary Figure 3

Examples of neurons recorded in MTL and MFC.

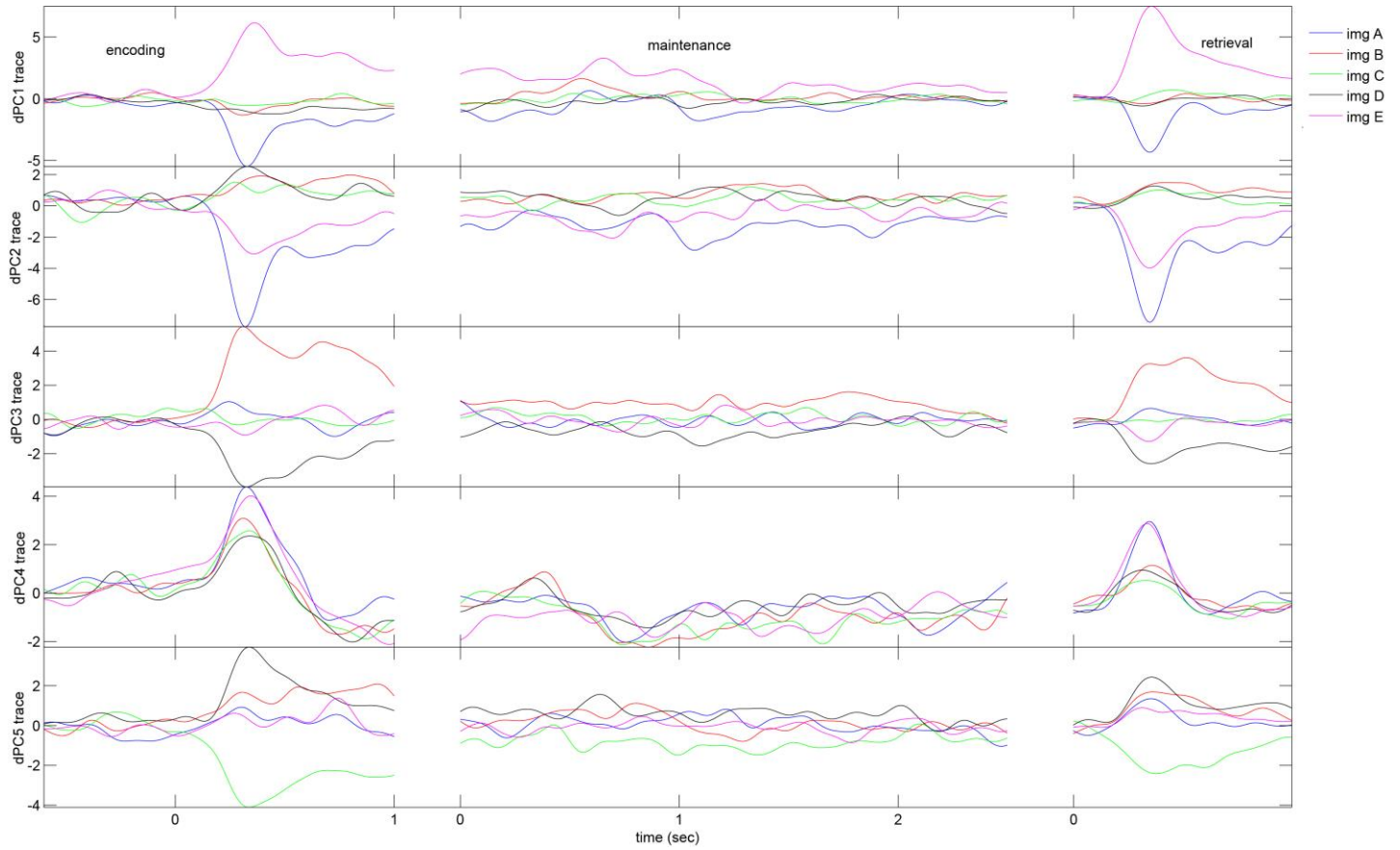
(a) Example of a concept cell recorded in the amygdala. Upper panel shows the PSTH (binsize 200ms, stepsize 2ms). Shaded areas represent s.e. across trials. Middle panel marks periods of significance between preferred vs. not preferred (corrected for multiple comparisons using a cluster-size correction, see methods). Bottom panel shows raster with trials re-ordered according to condition for plotting purposes only. This unit shows both visually evoked selective activity (red) and sustained activity (blue) during maintenance. Note how during maintenance, concept cells have elevated activity only when their preferred stimulus was held in memory (blue vs. gray). Also note how the sustained activity (blue) was suppressed during encoding of the non-preferred image (i.e. encoding 3) when the preferred stimulus was already held in memory. (b) Second example of a concept cell recorded in the amygdala. Notation is same than in (a). (c) Neuron which modulated its persistent activity as a function of load. (d) Example of neuron which modulated its persistent activity as a function of response speed (correct trials only).



Supplementary Figure 4

Separability of neuronal classes and effects of epilepsy

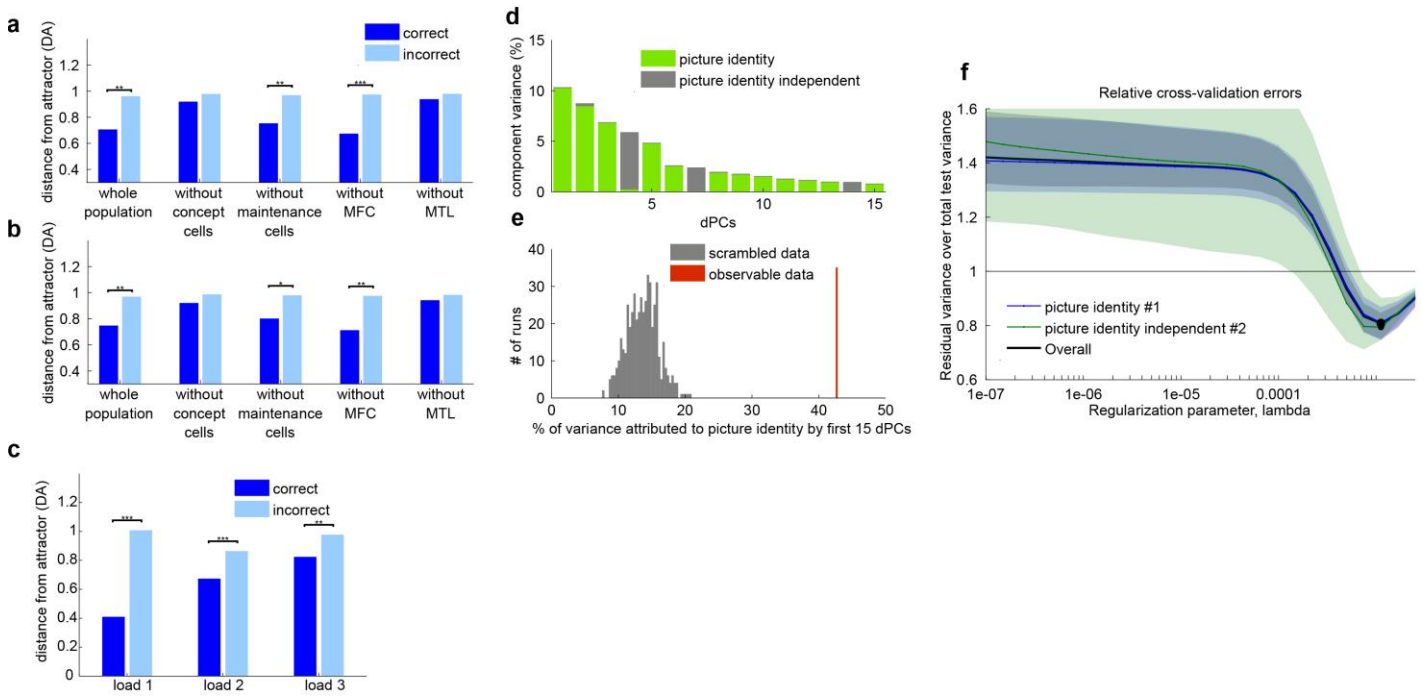
(a) Overlap of three neuronal classes we identified. The number of cells which qualified as both concept and maintenance cells was not larger than that expected if the two groups were independent (n=13, 14% of all concept cells, Fisher's exact test, P=0.201). Similarly, cells that qualified both as concept and probe cells were few and not more than expected from independence (n=7, 7% of all concept cells, Fisher's exact test, P=0.223). The percentage of maintenance cells that was classified as probe cells was 17% (N=22, Fisher exact test marginally significant, P=0.044). Nevertheless, most of the maintenance neurons (N=104) where not classified as probe neurons. (b) We verified whether the groups we identified truly constitute separate categories. Alternatively, they might represent the tails of a continuous distribution. To test this, we computed correlations between the effect sizes attributed to the selection criteria for each cell type. We used the t-statistic that were used to identify the different neuron classes as the effect size (see methods). We found no significant correlation between the effect sizes for image identity and maintenance selectivity for concept cells, maintenance cells, or all recorded cells (r=0.13; P=0.26, r=0.03; P=0.97; r=0.059; p=0.13, respectively). The marginal distributions show the density of observed values for each cell type (color-code as indicated). (c) Similarly, we found no significant correlation between the effect sizes for image selectivity and probe selectivity for concept cells, maintenance cells, or all recorded cells (r=-0.03; p=0.779, r=-0.0259; p=0.794,r-0.042; p=0.28, respectively). Lastly, we found no significant correlation between the effect sizes for probe and maintenance selectivity for maintenance cells, probe cells, and all recorded cells (r=-0.0259 p=0.794, r=0.078; P=0.5,r-0.043 p=0.27, respectively). Together, this shows that the three cell groups we quantified are largely distinct and non-overlapping. (a) Boxplot represents quartiles (25%, 75%), line is median, whiskers show range up to 1.5 times the interquartile range, and dots above whiskers show outliers. (d) We determined whether the effects observed in single unit analysis differed as a function of whether the neurons were recorded in tissue that was later determined to be epileptic or not (see Supplementary table 1). We labeled a neuron as located in a putative "epileptic" part of the brain if it was located in the same area as an electrophysiologically identified focus (of which a patient might have several; all were labeled epileptic for patients with generalized epilepsy). There was no significant difference in PSI (permuted t-test t[76]=0.66 P=0.38) for concept cells. We also found no difference in the proportion of load selective neurons (epileptic tissue 25% vs. non-epileptic: 34%, $chi^2[1]=0.021$; P=0.88), and no difference in the proportion of cell showing selectivity for RT during maintenance (epileptic tissue 7% vs. non-epileptic: 20%, $chi^2[1]=1.45$; P=0.22).



Supplementary Figure 5

Details of the dimensionality reduction technique (dPCA) used for state-space analysis

The first five demixed principal components (dPCs) in the different phases of the task during load 1. Colors denote the five different images. Note how dPCs 1,2,3 and 5 separate the different images. In contrast, dPC 4 was only modulated as a function of time but not image identity. Consequently, we did not include dPC 4 in Fig. 7.



Supplementary Figure 6

Controls and supplementary results for state-space analysis and dimensionality reduction.

(a,b) Same analysis as shown in Fig. 8f, but using the first 8 (a) or 12 (b) dPCs for which the highest percentage was attributed to image identity. Similar to Fig. 8f, where we used the first 4 dPCS, the distance to the attractor (DA) was significantly smaller for correct compared to incorrect trials only when concept cells were part of the. (c) The distance to the attractor (DA) for correct vs. incorrect trials separately for each load. The DA remains significantly smaller for correct compared to incorrect trials for all loads. (d) Percent variance explained by the first 15 dPCs. Each bar also contains information about the proportion of variance of each dPC attributable to image identity (green) and other factors (gray). Components 1,2,3,5,6, 8,9,10,11,12,13,15 have the highest percent of variance attributable to picture identity. (e) The observed percent of explained variance attributed to image identity by the first 15 dPCs (red) was significantly larger than that for data where we randomly scrambled image identity before performing the dPCA (P=0.002). This shows that the dPCA did not overfit. (f) Regularization of the dimensionality reduction technique (dPCA) used for state-space analysis. Shown is the cross-validation error as a function of the regularization parameter lambda. The black dot denotes the lambda value we used for all analysis.

ID	Age	Sex	Epilepsy diagnosis
P 31C	32	M	Left temporal neocortical
P 32C	19	M	Not localized (generalized)
P 33C	44	F	Right temporal
P 34C	70	M	Bilateral temporal
P 35C	63	M	Left temporal neocortical
P 36C	45	M	Right Hippocampus
P 37C	33	F	Right Hippocampus
P 39C	26	M	Right insula
P 40C	25	M	Right motor cortex
P 47H	20	M	Right amygdala
P 48H	54	M	Left temporal
P 49H	54	F	Right amygdala and hipp
P 51H	24	M	Not localized (generalized)

Supplementary Table 1: List of patients. Age is at the time of recording. The diagnosis listed (focal epilepsy) was determined as a result of depth electrode monitoring.

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